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## (54) WETTABLE SILICONE HYDROGEL COMPOSITIONS AND METHODS FOR THEIR MANUFACTURE

ZUSAMMENSETZUNGEN VON BENETZBAREN SILICONHYDROGELS UND VERFAHREN ZU DEREN HERSTELLUNG

COMPOSITIONS D'HYDROGEL MOUILLABLE AU SILICONE ET PROCEDES DE FABRICATION DESDITES COMPOSITIONS

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## Description

The present invention relates to a method for improving the wettability of silicone-containing hydrogel compositions useful for the production of biomedical devices, especially contact lenses.

Hydrogels have been a desirable class of material for the preparation of biomedical devices, and have been known since at least Wichterle, et al U.S. Patent No. 3,220,960 which disclosed hydrogels comprising a hydrated polymer of a hydroxyalkyl acrylate or methacrylate crosslinked with a corresponding diester (poly 2-hydroxyethyl methacrylate, known as poly-HEMA).

A hydrogel is a hydrated crosslinked polymeric system that contains water in an equilibrium state. The physical properties of hydrogels can vary widely and are mostly determined by their water content. Since hydrogels exhibit excellent biocompatibility, there has been extensive interest in the use of hydrogels for biomedical devices, especially contact lenses.

In the field of contact lenses, various factors must combine to yield a material that has appropriate characteristics. Oxygen permeability, wettability, material strength and stability are but a few of the factors which must be carefully balanced to achieve a useable end-result contact lens. Since the cornea receives its oxygen supply exclusively from contact with the atmosphere, good oxygen permeability is a critical characteristic for any contact lens material.

It was discovered that certain crosslinked polymeric materials could be hydrated and retain their water content. It was further found that the higher the water content within contact lenses made from these crosslinked hydrogel polymers, the greater was the oxygen permeability through the lens to the cornea.

High water-containing hydrogels have at times exhibited undesirable mechanical properties. For example, such hydrogels are often not easily formed into hydrolytically stable lenses. Further such materials have at times exhibited tearing or other breakage as a result of poor tensile strength. What was needed was a highly oxygen permeable material that was durable and highly wettable. Wettability is important in that, if the lens is not sufficiently wettable, it does not remain lubricated and therefore cannot be worn comfortably in the eye. The optimum contact lens would have not only excellent oxygen permeability, but also excellent tear fluid wettability.

Silicone-containing materials were tried as viable contact lens materials and displayed very good oxygen permeability and durability. However, most silicone-containing materials are largely hydrophobic and therefore not sufficiently wettable. Further, it is believed that such hydrophobicity causes enhanced deposit problems, which may also result in discomfort when wearing contact lenses made from certain silicone-containing polymers.

Therefore, an optimal hydrogel material for biomedical devices, such as contact lenses, would have ideal rigidity, high oxygen permeability and a high degree of wettability.

In accordance with this invention, it has now been discovered that the surface wettability of silicone-containing hydrogels, and more specifically polyurethane-silicone hydrogels and ethylenically terminated polysiloxane hydrogels such as (poly)organosiloxane hydrogels, are significantly enhanced by incorporating specific vinyl-containing hydrophilic monomers together with a specific acrylic-containing hydrophilic monomer into the monomer mix along with the silicone-containing monomer or prepolymer.

Thus, the present invention provides a method for improving the wettability of silicone-containing hydrogels comprising the steps of (a) forming a monomer mix comprising at least one silicone-containing monomer, N,N-dimethylacrylamide and a vinyl-containing monomer selected from N-vinylpyrrolidone, N-vinyl-N-methyl acetamide, N-vinyl-N-ethyl acetamide, N-vinyl-N-methyl formamide, and N-vinyl formamide, and (b) curing the monomer mix of step (a) to form a silicone-containing hydrogel with improved wetting properties.

It is believed that the combined vinyl-containing monomers and N,N-dimethylacrylamide monomer act as wetting agents, and interact with the predominantly hydrophobic silicone-containing monomers and prepolymers in the monomer mix to produce highly wettable hydrogels with ideal rigidity. Such resultant hydrogels are especially well-suited for use as contact lens materials.

## BRIEF DESCRIPTION OF THE DRAWINGS

Figures 1 and 2 depict the effect on modulus of polyurethane films as the composition ratio of NVP to DMA is changed.

Figure 3 depicts the effect on modulus of methacrylate-capped polysiloxane films as the composition ratio of NVP to DMA is changed.

## DETAILED DESCRIPTION OF THE INVENTION

Silicone hydrogels (i.e., hydrogels containing silicone) are usually prepared by polymerizing a mixture containing at least one silicone-containing monomer and at least one hydrophilic monomer. Either the silicon -containing monomer or the hydrophilic monomer may function as a crosslinking agent (a crosslinker being defined as a monomer having

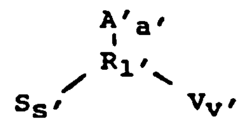
multiple polymerizable functionalities) or a separate crosslinker may be employed.

The vinyl-containing monomers used with the silicone-containing monomers in the method of the present invention are N-vinyl pyrrolidone, N-vinyl-N-methyl acetamide, N-vinyl-N-ethyl acetamide, N-vinyl-N-methyl formamide, N-vinyl formamide, with N-vinyl pyrrolidone (NVP) being preferred.

The third essential monomer component of the monomer mix is N,N-dimethyl (meth)acrylamide (DMA).

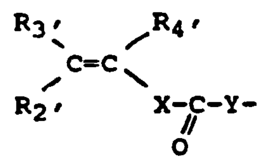
It is preferable to add a crosslinking composition containing at least one vinyl-containing polymerizable group and at least one acrylic- or styrene-containing polymerizable group disclosed in copending and commonly assigned U.S. Application No. 07/788,071 filed November 5, 1991 and having the following general schematic representation (I):

(I)



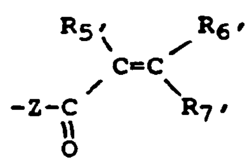
wherein:

V denotes



;

A' denotes



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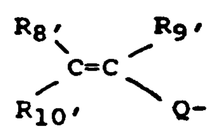
S denotes



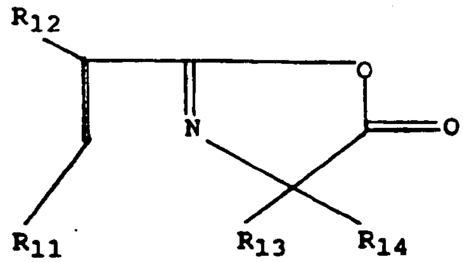
;

| | |
|---|---|
| $R_{1'}$ | is an alkyl radical derived from substituted and unsubstituted hydrocarbons, polyalkylene oxide, poly (perfluoro) alkylene oxide, dialkyl-capped polydimethylsiloxane, dialkyl-capped polydimethylsiloxane modified with fluoroalkyl or fluoroether groups; |
| $R_{2'}$-$R_{10'}$ | are independently H, or alkyl of 1 to 5 carbon atoms; |
| Q | is an organic group containing aromatic moieties having 6 to 30 carbon atoms; |
| X, Y, and Z | are independently O, NH or S; |
| v' | is 1, or higher; and |
| a', s' | independently are greater than or equal to 0, and $a' + s' \geq 1$. |

A preferred crosslinking agent is methacryloxyethyl vinyl carbonate.

The addition of crosslinking agents of Formula I assists in the copolymerization of the vinyl-containing monomers and N,N-dimethylacrylamide with each other as well as with other monomers and prepolymers present in the monomer mix, such as the relatively non-polar ring-containing oxazolone compounds of the general formula (II):

(II)



where

$R_{11}$ and $R_{12}$ independently denote H or $CH_3$; and
$R_{13}$ and $R_{14}$ independently denote methyl or cyclohexyl radicals.

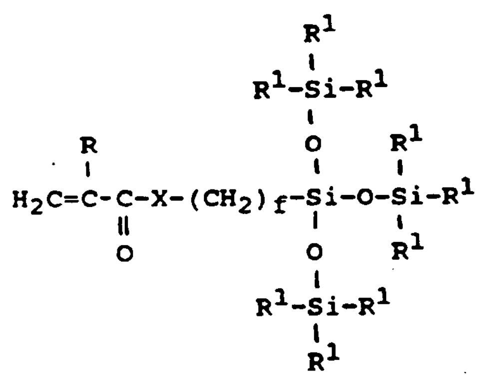
These ring-containing monomers which may be incorporated into the silicone-containing hydrogels of the present invention specifically include 2-isopropenyl-4,4-dimethyl-2-oxazolin-5-one (IPDMO), 2-vinyl-4,4-dimethyl-2-oxazolin-5-one (VDMO), cyclohexane spiro-4'-(2'isopropenyl-2'-oxazol-5'-one) (IPCO), cyclohexane-spiro-4'-(2'-vinyl-2'oxazol-5'-one) (VCO), and 2-(-1-propenyl)-4,4-dimethyl-oxazol-5-one (PDMO). The preferred oxazolones are prepared by known reaction sequences set forth in commonly assigned U.S. Patent No. 4,810,764. The amount of crosslinker used is about 0.01 to about 5% of the vinyl-containing monomer weight present in a useful formulation.

Any known silicone-containing prepolymer may be used to form the silicone hydrogels of this invention, as will be apparent to one skilled in the art. The monomers added to the monomeric mixture may be monomers or prepolymers. A "prepolymer" is a reaction intermediate polymer of medium molecular weight having polymerizable groups. Thus it is understood that the terms "silicone-containing monomers" and "hydrophilic monomers" include prepolymers. Examples of such monomers may be found in United States Patent Nos. 4,136,250; 4,153,641; 4,740,533; 5,034,461; and 5,070,215.

Further, notations such as "(meth)acrylate or "(meth)acrylamide are used herein to denote optional methyl substitution. Thus, for example, methyl (meth)acrylate includes both methyl acrylate and methyl methacrylate.

One preferred class of suitable silicone-containing monomers are bulky polysiloxanylalkyl (meth)acrylic monomers represented by the formula (III):

(III)



wherein:

X is O or NR;
each R is independently hydrogen or methyl; and
each $R^1$ is independently a lower alkyl or phenyl group; and
f is 1 or 3 to 10.

Such bulky monomers include methacryloxypropyl tris(trimethylsiloxy)silane, pentamethyldisiloxanylmethylmethacrylate, tris(trimethylsiloxy)methacryloxy propylsilane, phenyltetramethyldisiloxanylethyl acetate, and methyldi

(trimethylsiloxy)methacryloxymethyl silane.

A further preferred class of silicon -containing monomers are the poly(organosiloxane) prepolymers represented by the formula (IV):

$$\text{(IV)}\qquad A-(R^7)-\underset{R^4}{\overset{R^3}{\underset{|}{\overset{|}{Si}}}}-[O-\underset{R^6}{\overset{R^5}{\underset{|}{\overset{|}{Si}}}}]_n-O-\underset{R^4}{\overset{R^3}{\underset{|}{\overset{|}{Si}}}}-(R^7)-A$$

wherein:

A is an activated unsaturated group, such as an ester or amide of an acrylic or a methacrylic acid;
each $R^3$-$R^6$ is independently selected from the group consisting of a monovalent hydrocarbon radical or a halogen substituted monovalent hydrocarbon radical having 1 to 18 carbon atoms which may have ether linkages between carbon atoms;
$R^7$ is a divalent hydrocarbon radical having from 1 to 22 carbon atoms;
and
n is 0 or an integer greater than or equal to 1.

A further preferred class of silicone-containing monomers are the monomers having the following schematic representations:

$$\text{(V)}\qquad E(*D*A''*D*G)_a*D*A''*D*E';$$

or

$$\text{(VI)}\qquad E(*D*G*D*A'')_a*D*G*D*E';$$

where

D denotes an alkyl diradical, an alkyl cycloalkyl diradical, a cycloalkyl diradical, an aryl diradical or an alkylaryl diradical having 6 to 30 carbon atoms;
G denotes an alkyl diradical, a cycloalkyl diradical, an alkyl cycloalkyl diradical, an aryl diradical or an alkylaryl diradical having 1 to 40 carbon atoms and which may contain ether, thio or amine linkages in the main chain;
* denotes a urethane or ureido linkage;
a is at least 1;
A" denotes a divalent polymeric radical of formula (VII):

$$\text{(VII)}\qquad -(CH_2)_m-\left[\underset{R^{s'}}{\overset{R^s}{\underset{|}{\overset{|}{Si}}}}-O\right]_p-\underset{R^{s'}}{\overset{R^s}{\underset{|}{\overset{|}{Si}}}}-(CH_2)_m-$$

wherein:

$R^s$ and $R^{s'}$ independently denote an alkyl or fluoro-substituted alkyl group having 1 to 10 carbon atoms which may contain ether linkages between carbon atoms;
m is at least 1; and
p provides a moiety weight of 400 to 10,000;

E and E' independently denote a polymerizable unsaturated organic radical represented by formula (VIII):

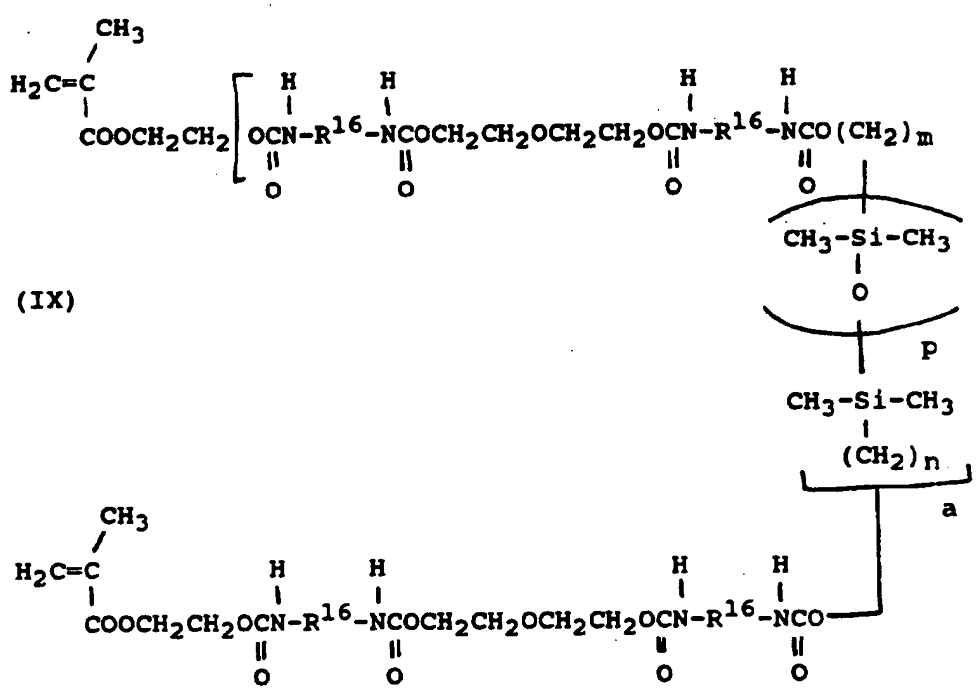
$$\text{(VIII)}\qquad R^{13}-CH=\overset{R^{12}}{\overset{|}{C}}-(CH_2)_w-(X)_x-(Z)_z-(Ar)_y-R^{14}-$$

wherein:

$R^{14}$ denotes a divalent alkylene radical having 1 to 10 carbon atoms;

$R^{12}$ denotes H or $CH_3$;
$R^{13}$ denotes H, a ($C_1$-$C_6$) alkyl radical or a -CO-Y-$R^{15}$ group wherein Y is -O-, -S- or -NH- and $R^{15}$ is a alkyl radical having 1 to 12 carbon atoms;
X is -CO- or -OCO-;
Z is -O- or -NH-;
Ar denotes an aromatic radical having 6 to 30 carbon atoms;
w is 0 to 6;
x is 0 or 1;
y is 0 or 1; and
z is 0 or 1.

A preferred urethane monomer is represented by formula (IX):



(IX)

wherein:

$R^{16}$ is a diradical of a diisocyanate after removal of the isocyanate group, and is most preferably the diradical of isophorone diisocyanate, and m, p and a are the same as previously defined. Preferably, the sum of m and a is 3 or 4, and more preferably, a is 1 and m is 3 or 4. Preferably, p is at least 30.

The wettable silicone-containing hydrogels of the present invention, when used in contact lens applications, can produce a wide variety of types of hydrogel contact lenses. As is understood in the field, in general, hydrogel contact lenses should have oxygen permeabilities with DK values greater than about 20 x $10^{-11}$ $cm^3$ x cm/sec x $cm^2$ x mmHg (or 20 DK units) and preferably greater than about 60 DK. They should have a Young's modulus of elasticity in the range of about 5 to 400 g/$mm^2$, preferably greater than about 20g/$mm^2$ as measured by ASTM test method D1938. Their water content should be between about 10 and 80 %, and preferably between 20 and 60%. The contact angle, which is a measurement of the wettability of the lens, should be less than about 80 degrees and should preferably be less than about 40 degrees.

The preferred range of the combined vinyl-containing and hydrophilic monomer and N,N-dimethylacrylamide concentration is from about 5 weight percent of the polymeric hydrogel mix to about 80 weight percent, and more preferably from about 20 weight percent to about 60 weight percent. The weight ratio of vinyl-containing monomer to N,N-dimethylacrylamide is from about 40:1 to about 1:40, and is preferably higher than 1:1.

The present inv ntion further provides articles of manufacture which can be used for biomedical devices, such as, contact lenses, surgical devices, heart valves, vessel substitutes, intrauterine devices, membranes and other films, diaphragms, surgical implants, blood vessels, artificial ureters, artificial breast tissue and membranes intended to come into contact with body fluid outside of the body, .g., membranes for kidney dialysis and heart/lung machines, catheters, mouth guards, denture liners, intraocular devices, and especially contact lenses.

It is known that blood, for example, is readily and rapidly damaged when it comes into contact with artificial surfaces. The design of a synthetic surface which is antithrombogenic and nonhemolytic to blood is necessary for prostheses and devices used with blood.

The terms "shaped articles for use in biomedical applications" or "biomedical devices" mean the materials disclosed herein have physicochemical properties rendering them suitable for prolonged contact with living tissue, blood and the mucous membranes.

Although the exact mechanisms are not fully understood at the present time, the wetting agents used in the present invention appear to reduce the deposition problems normally associated with, and believed to be caused by, the high hydrophobicity of the hydrophobic silicone-containing monomers.

Further, the wetting agents of the present invention significantly reduce the contact angle of the surface - a clear indication to those skilled in the field that enhanced wetting has occurred. The resulting novel hydrogels comprising the wetting agents of the present invention were unexpectedly hydrolytically stable, within an acceptable range, while collecting only an acceptable level of deposits.

Two preferred classes of silicone-containing monomers contemplated by the present invention are urethane-containing prepolymers, and ethylenically terminated polysiloxane containing monomers as previously described herein, such as, most preferably $\alpha,\omega$ bis(methacryloxyalkyl)polysiloxane.

The resulting polymers and copolymers disclosed herein can be boiled and/or autoclaved in water without being damaged whereby sterilization may be achieved. Thus, an article formed from the disclosed polymers and copolymers may be used, for example, in surgery where an article is needed which is compatible with living tissue or with the mucous membranes.

The monomer mixes employed in this invention, can be readily cured to cast shapes by conventional methods such as UV polymerization, or thermal polymerization, or combinations thereof, as commonly used in polymerizing ethylenically unsaturated compounds. Representative free radical thermal polymerization initiators are organic peroxides, such as acetal peroxide, lauroyl peroxide, decanoyl peroxide, stearoyl peroxide, benzoyl peroxide, tertiarybutyl peroxypivalate and peroxydicarbonate, employed in a concentration of about 0.01 to 1 percent by weight of the total monomer mixture. Representative UV initiators are those known in the field such as, benzoin methyl ether, benzoin ethyl ether, Darocure 1173, 1164, 2273, 1116, 2959, 3331 (EM Industries) and Irgacure 651 and 184 (Ciba-Geigy).

Polymerization of the monomer mix of this invention may be performed in the presence of a diluent. The polymerization product will then be in the form of a gel. If the diluent is nonaqueous, the diluent must be removed from the gel and replaced with water through the use of extraction and hydration protocols well known to those skilled in the art.

It is also possible to perform the polymerization in the absence of diluent to produce a xerogel. These xerogels may then be hydrated to form the hydrogels as is well known in the art.

In addition to the above-mentioned polymerization initiators, the copolymer of the present invention may also include other monomers as will be apparent to one skilled in the art. For example, the monomer mix may include additional hydrophilic monomers, colorants, curing agents, or UV-absorbing and toughening agents such as those known in the contact lens art.

The polymers of this invention can be formed into contact lenses by spincasting processes (such as those disclosed in U.S. Pat. Nos. 3,408,429 and 3,496,254), cast molding processes (such as those disclosed in U.S. Pat. Nos. 4,084,459 and 4,197,266), combinations of methods thereof, or any other known method for making contact lenses. Polymerization may be conducted either in a spinning mold, or a stationary mold corresponding to a desired contact lens shape. The lens may be further subjected to mechanical finishing, as occasion demands. Polymerization may also be conducted in an appropriate mold or vessel to form buttons, plates or rods, which may then be processed (e.g., cut or polished via lathe or laser) to give a contact lens having a desired shape.

The hydrogels the present invention are oxygen transporting, hydrolytically stable, biologically inert, and transparent. The monomers and prepolymers employed in accordance with this invention, are readily polymerized to form three dimensional networks which permit the transport of oxygen and are optically clear, strong and hydrophilic.

The relative softness or hardness of the contact lenses fabricated from the resulting polymer of this invention can be varied by decreasing or increasing the molecular weight of the polysiloxane prepolymer endcapped with the activated unsaturated group or by varying the percent of the comonomer. As the ratio of polysiloxane units to end-cap units increases, the softness of the material increases.

The following examples serve to illustrate the present invention.

The following abbreviations used are defined as follows:

NVP is N-vinyl pyrrolidone
DMA is N,N-dimethyl acrylamide
HEMAVc is methacryloxyethyl vinyl carbonate
TRIS is methacryloxypropyl tris(trimethylsiloxy)silane
IDS3H is a urethane prepolymer derived from isophorone diisocyante, diethylene glycol, polysiloxanediol encapped with 2-hydroxyethyl methacrylate
$M_2D_x$ is an $\alpha,\omega$ -bis(methacryloxyalkyl)polysiloxane
VDMO is 2-vinyl-4,4-dimethyl-2-oxazoline-5-one

**EXAMPLES 1-6**

Polyurethane-silicone Hydrogels

Six polyurethane hydrogel films containing the following ingredients, were prepared:

a) IDS3H, 30 parts;
b) TRIS, 30 parts;
c) NVP, varied from 0 to 40 parts;
d) DMA, varied from 40 to 0 parts (NVP + DMA = 40 parts)
e) Methacryloxyethylvinyl carbonate (HEMAVc crosslinker) at 0.3% of NVP amount;
f) n-Hexanol 40 parts;
g) Darocur-1173, (UV initiator), 0.2 part.

These formulations were UV cured, followed by ethanol extraction and boiling water hydration, as is known in the art, to give resultant hydrogel films with the following properties (water content and modulus). Figure 1 depicts the resultant films of Examples 1-6 with one plotted point for each film respectively.

Table 1

| EXAMPLE | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| NVP/DMA ratio | 40/0 | 38/2 | 35/5 | 30/10 | 20/20 | 0/40 |
| % water | 35 | 46 | 44 | 41 | 41 | 37 |
| Modulus | 430 | 281 | 150 | 80 | 79 | 63 |

The modulus/composition relationship is depicted in Figure 1.

**EXAMPLE 7**

Polyurethane Hydrogel

A formulation was prepared containing the same ingredients and same weight ratios as those in Example 4, except that 3 parts of NVP and 1 part of DMA was replaced by 1 part of VDMO. The formulation was cast onto films and processed as done in Examples 1-6. The resulting hydrogel films had the following properties: water content, 40%; modulus 110 g/mm$^2$.

**EXAMPLES 8 - 11**

Polyurethane-silicone Hydrogels

Polyurethane formulations of the ingredients as in Examples 1-6 but of different relative parts, as shown in Table 2, were prepared.

a) IDS3H & b) TRIS, 34 parts each;
c) NVP & d) DMA, 32 parts combined;
e) n-Hexanol, f) HEMAVc and g) Darocure-1173, same parts as in Examples 1-6.

The formulations were cast and processed in the same manner as in Examples 1-6, with the water content and

modulus data shown in Table 2. Figure 2 depicts the resultant films of Examples 8-11, with one plotted point representing each film respectively.

Table 2

| EXAMPLE | 8 | 9 | 10 | 11 |
|---|---|---|---|---|
| NVP/DMA ratio | 32/0 | 24/8 | 16/16 | 0/32 |
| water % | 25 | 26 | 31 | 25 |
| Modulus | 610 | 275 | 107 | 87 |

The modulus/composition relationship is further shown in Figure 2.

**EXAMPLES 12-15**

$M_2D_x$-based Hydrogel Films

The following silicone hydrogel formulations were prepared and cast processed into hydrogel films by the procedure of Examples 8-11. Figure 3 depicts the resultant films of Examples 8-11, with one plotted pointrepresenting each film respectively. The ingredients in the formulation were:

a) $M_2D_x$, 13 parts
b) TRIS, 47 parts
c) NVP & d) DMA, 40 parts combined
e) n-Hexanol, 40 parts
f) HEMAVc, 0.3 part of NVP amount
g) Darocur, 0.2 part

The modulus-composition relationship is depicted in Figure 3.

**EXAMPLE 16**

Hydrogel Lens Casting

A monomer mix of the formulation as described in Examples 4, 9, 12 was filtered through a disposable 1.2 μm millipore filter into a clean vial. Under an inert nitrogen atmosphere, 60-90 μl of the mix was injected onto a clean plastic mold half and then covered with a second plastic mold half. The molds were then compressed and cured for 90 minutes in the presence of UV light (4200 microwatts/cm$^2$). The molds were then opened mechanically and put into a beaker containing aqueous ethanol. The lenses were released from the molds within 1 hour, then extracted with ethanol for 48 hours, and boiled in distilled water for 4 hours. The resultant lenses were inspected for cosmetic quality, cytotoxicity and dimensions. Lenses passing inspection were thermally disinfected in phosphate buffered saline prior to on-eye evaluation.

**EXAMPLE 17**

Clinical Evaluations

The cast-molded polyurethane lenses described in Example 12 were evaluated on six to ten patients. In each test, a poly(HEMA) control lens was worn on one eye and the test lens on the other eye. The lenses were analyzed after a minimum of one hour, and preferably 5 hours or longer for wettability and surface deposition study. The surface wettability rating scale was 0-4 with 0 representing 2/3 of the anterior surface unwetted by the tear film, and 4 representing complete wetting. The deposition scale was also 0-4 with 0 representing no surface deposits and 4 representing multiple deposits of 0.5 mm diameter or larger. The results for the lenses of the control formulation (according to Example 4) was 3.0 for wetting and 0.4 for deposits after five hours of wear. For lenses comprising 1 part of VDMO (Example 7 formulation), the results showed a wettability rating of 3.3 and a deposit rating of 0.7 after 5 hours or wear.

## Claims

1. A method for improving the wettability of silicone-containing hydrogels comprising the steps of (a) forming a monomer mix comprising at least one silicone-containing monomer, N,N-dimethylacrylamide and a vinyl-containing monomer selected from N-vinylpyrrolidone, N-vinyl-N-methyl acetamide, N-vinyl-N-ethyl acetamide, N-vinyl-N-methyl formamide, and N-vinyl formamide, and (b) curing the monomer mix of step (a) to form a silicone-containing hydrogel with improved wetting properties.

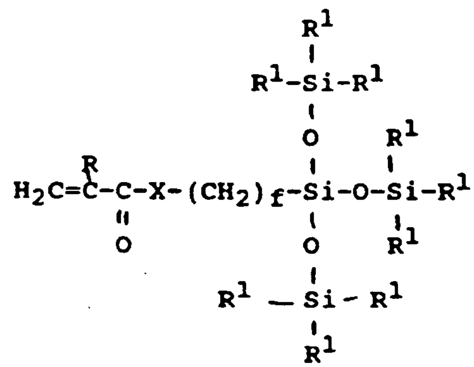
2. A method according to Claim 1, wherein said vinyl-containing monomer is N-vinylpyrrolidone.

3. A method according to Claim 1 or Claim 2, wherein said silicone-containing monomer is a urethane-containing prepolymer; an ethylenically terminated polysiloxane-containing prepolymer; a poly(organosiloxane) prepolymer represented by the formula:

$$A-(R^7)-\underset{R^4}{\overset{R^3}{Si}}-[O-\underset{R^6}{\overset{R^5}{Si}}]_n-O-\underset{R^4}{\overset{R^3}{Si}}-(R^7)-A$$

wherein:

A is an activated unsaturated groups;
each $R^3$-$R^6$ is independently selected from a monovalent hydrocarbon radical or a halogen substituted monovalent hydrocarbon radical having 1 to 18 carbon atoms which may have ether linkages between carbon atoms;
$R^7$ is a divalent hydrocarbon radical having from 1 to 22 carbon atoms; and
n is 0 or an integer greater than or equal to 1; or a bulky polysiloxanylalkyl (meth)acrylic monomer having the formula:



wherein:
X is O or NR;
each R is independently hydrogen or methyl; and
each $R^1$ is independently a lower alkyl or phenyl group; and
f is 1 or 3 to 10.

4. A method according to Claim 3, wherein said bulky polysiloxanyalkyl (meth)acrylate monomer is selected from methacryloxypropyl tris(trimethylsiloxy)silane, pentamethyldisiloxanylmethylmethacrylate, tris(trimethylsiloxy) methacryloxy propylsilane, phenyltetramethyldisiloxanylethyl acetate, and methyldi(trimethylsiloxy)methacryloxymethyl silane.

5. A method according to Claim 3, wherein said silicone-containing monomer is a urethane-containing prepolymer having the following schematic representation:

$$E(*D*A''*D*G)_a*D*A''*D*E';$$

or

$$E(*D*G*D*A'')_a*D*G*D*E';$$

wherein

D denotes an alkyl diradical, an alkyl cycloalkyl diradical, a cycloalkyl diradical, an aryl diradical or an alkylaryl diradical having 6 to 30 carbon atoms;
G denotes an alkyl diradical, a cycloalkyl diradical, an alkyl cycloalkyl diradical, an aryl diradical or an alkylaryl diradical having 1 to 40 carbon atoms and which may contain ether, thio or amine linkages in the main chain;
* denotes a urethane or ureido linkage;
a is at least 1;
A" denotes a divalent polymeric radical of the formula:

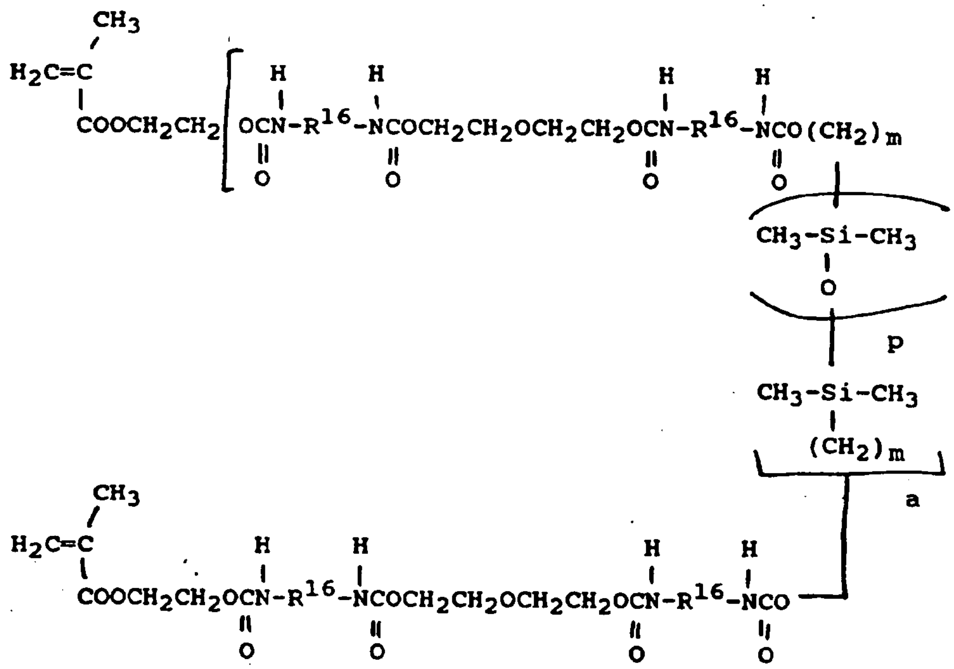
$$-(CH_2)_m-\left[\begin{matrix} R^s \\ | \\ Si-O \\ | \\ R^{s'} \end{matrix}\right]_p-\begin{matrix} R^s \\ | \\ Si \\ | \\ R^{s'} \end{matrix}-(CH_2)_m-$$

wherein
$R^s$ and $R^{s'}$ independently denote an alkyl or fluoro-substituted alkyl group having 1 to 10 carbon atoms which may contain ether linkages between carbon atoms;
m is at least 1; and
p provides a moiety weight of 400 to 10,000;
E and E' independently denote a polymerizable unsaturated organic radical represented by the formula:

$$R^{13}-CH=\overset{\displaystyle R^{12}}{\overset{|}{C}}-(CH_2)_w-(X)_x-(Z)_z-(Ar)_y-R^{14}-$$

wherein:
$R^{14}$ denotes a divalent alkylene radical having 1 to 10 carbon atoms;
$R^{12}$ denotes H or $CH_3$;
$R^{13}$ denotes H, a $(C_1\text{-}C_6)$ alkyl radical or a -CO-Y-$R^{15}$ group wherein Y is -O-, -S- or -NH- and $R^{15}$ is an alkyl radical having 1 to 12 carbon atoms;
X is -CO- or -OCO-;
Z is -O- or -NH-;
Ar denotes an aromatic radical having 6 to 30 carbon atoms;
w is 0 to 6;
x is 0 or 1;
y is 0 or 1; and
z is 0 or 1.

6. A method according to Claim 5, wherein said urethane-containing prepolymer is represented by the formula:



wherein:

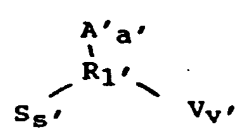
$R^{16}$ is a diradical of a diisocyanate after removal of the isocyanate group and m, p and a are the same as previously defined.

7. A method according to any preceding claim, wherein said monomer mix comprises N,N-dimethylacrylamide and N-vinyl pyrrolidone.

8. A method according to Claim 7, wherein said monomer mix comprises either a urethane-containing prepolymer or an ethylenically terminated polysiloxane-containing monomer.

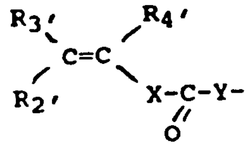
9. A method according to any preceding claim, wherein said monomer mix further comprises a relatively non-polar ring-containing compound selected from 2-vinyl-4,4-dimethyl-2-oxazolin-5-one, 2-isopropenyl-4,4-dimethyl-2-oxazolin-5-one, cyclohexane-spiro-4'-(2'-isopropenyl-2'-oxazol-5'-one), cyclohexane-spiro-4'-(2'-vinyl-2'-oxazol-5'-one) and 2-(1-propenyl)-4,4-dimethyloxazol-5-one.

10. A method according to any preceding claim, wherein said monomer mix further comprises a crosslinking agent having the general schematic representation:



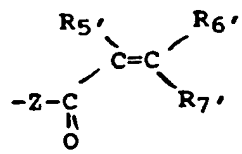
wherein

V denotes



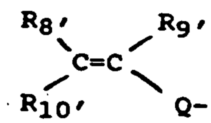
;

A' denotes



;

S denotes



;

$R_{1'}$ is an alkyl radical derived from substituted and unsubstituted hydrocarbons, polyalkylene oxide, poly(perfluro) alkylene oxide, dialkyl-capped polydimethylsiloxane, dialkyl-capped polydimethylsiloxane modified with fluoroalkyl or fluoroether groups;
$R_{2'}$-$R_{10'}$ are independently H, or alkyl of 1 to 5 carbon atoms;
Q is an organic group containing aromatic moieties having 6 to 30 carbon atoms;
X, Y and Z are independently O, NH or S;
v' is 1, or higher; and
a', s' are independently greater than or equal to 0, and a' + s' ≥ 1.

11. The method of Claim 10, wherein said crosslinking agent is methacryloxyethyl vinyl carbonate.

12. A silicon-containing hydrogel composition formed by a method according to any preceding claim.

13. A biomedical device made from a hydrogel composition according to Claim 12.

14. A contact lens according to Claim 13.

**Patentansprüche**

1. Eine Methode zum Verbessern der Benetzbarkeit von silikonhaltigen Hydrogelen, die die Schritte (a) der Rildung einer Monomermischung, die mindestens ein silikonhaltiges Monomer, N,N-Dimethylacrylamid und ein vinylhaltiges Monomer enthält, ausgewählt aus N-Vinylpyrrolidon, N-Vinyl-N-Methylacetamid, N-Vinyl-N-Ethylacetamid, N-Vinyl-N-Methylformamid, und (b) der Aushärtung der Monomermischung von Schritt (a) zur Bildung eines silikonhaltigen Hydrogels mit verbesserten Benetzungseigenschaften umfaßt.

2. Eine Methode nach Anspruch 1, in der besagtes vinylhaltiges Monomer N-Vinylpyrrolidon ist.

3. Eine Methode nach Anspruch 1 oder Anspruch 2, in der besagtes silikonhaltiges Monomer ein urethanhaltiges Prepolymer, ein ethylenisch abgeschlossenes, polysiloxanhaltiges Prepolymer, ein Poly(organosiloxan)-Prepolymer ist, dargestellt durch die Formel:

$$\begin{array}{ccccccc} & & R^3 & & R^5 & & R^3 \\ & & | & & | & & | \\ A-(R^7)- & & Si & -[O- & Si & ]_n-O- & Si & -(R^7)-A \\ & & | & & | & & | \\ & & R^4 & & R^6 & & R^4 \end{array}$$

worin

A eine aktivierte, ungesättigte Gruppe ist,
jedes $R^3$-$R^6$ unabhängig voneinander ausgewählt ist aus einem einwertigen Kohlenwasserstoffradikal oder einem halogensubstituierten, einwertigen Kohlenwasserstoffradikal mit 1 bis 18 Kohlenstoffatomen, das Etherverbindungen zwischen Kohlenstoffatomen haben kann,
$R^7$ ein zweiwertiges Kohlenwasserstoffradikal mit 1 bis 22 Kohlenstoffatomen ist, und
n 0 oder eine ganze Zahl größer oder gleich 1 ist oder ein voluminöses Polysiloxanylalkyl-(Meth)acryl-Monomer mit der Formel:

$$H_2C{=}C(R)-C({=}O)-X-(CH_2)_f-Si[O-Si(R^1)_3]_2-O-Si(R^1)_2-R^1$$

worin
X O oder NR ist,
jedes R unabhängig voneinander Wasserstoff oder Methyl ist, und
jedes $R^1$ unabhängig voneinander eine niedrigere Alkyl- oder Phenylgruppe ist, und
f 1 oder 3 bis 10 ist.

4. Eine Methode nach Anspruch 3, in der besagtes voluminöses Polysiloxanyl-(Meth)acryl-Monomer ausgewählt ist aus Methacryloxypropyl-Tris(trimethylsiloxy)silan, Pentamethyldisiloxyanylmethylmethacrylat, Tris(trimethylsiloxy)methacryloxypropylsilan, Phenyltetramethyldisiloxyanylethylacetat und Methyldi(trimethylsiloxy)methacryloxymethylsilan.

5. Eine Methode nach Anspruch 3, in der besagtes silikonhaltiges Monomer ein urethanhaltiges Prepolymer mit, der folgenden schematischen Darstellung ist:

$$E(*D*A''*D*G)_a*D*A''*D*E'$$

oder

$$E(*D*G*D*A'')_a*D*G*D*E',$$

worin

D ein Alkyl-Diradikal, ein Alkylcycloalkyl-Diradikal, ein Cycloalkyl-Diradikal, ein Aryl-Diradikal oder ein Alkylaryl-Diradikal mit 6 bis 30 Kohlenstoffatomen bedeutet,
G ein Alkyl-Diradikal, ein Cycloalkyl-Diradikal, ein Alkylcycloalkyl-Diradikal, ein Aryl-Diradikal oder ein Alkylaryl-Diradikal mit 1 bis 40 Kohlenstoffatomen bedeutet, und das Ether-, Thio- oder Aminverbindungen in der Hauptkette enthalten kann,
* eine Urethan- oder Ureidverbindung bedeutet,
a mindestens 1 ist,
A'' ein zweiwertiges Polymerradikal bedeutet mit der Formel:

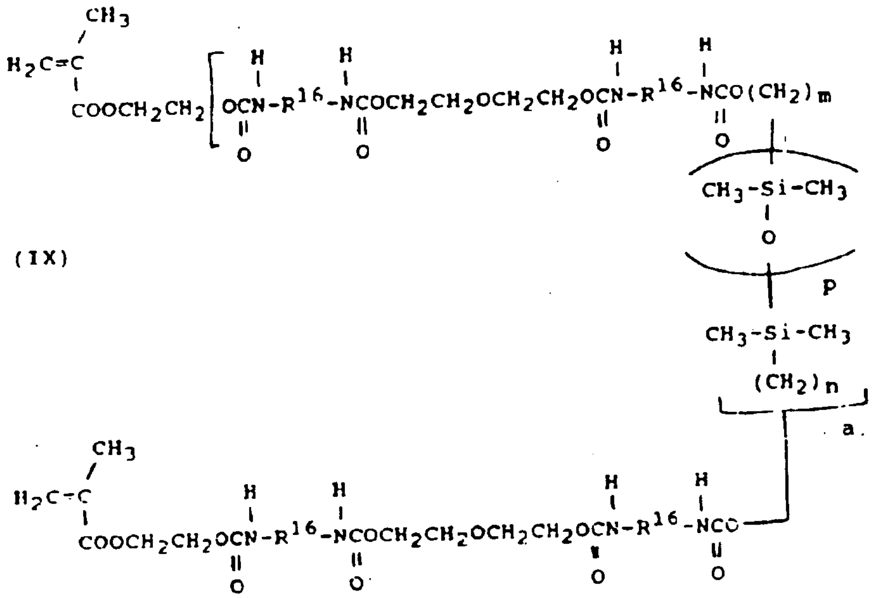
$$-(CH_2)_m-\left[\begin{array}{c} R^s \\ | \\ Si-O \\ | \\ R^{s'} \end{array}\right]_p-\begin{array}{c} R^s \\ | \\ Si \\ | \\ R^{s'} \end{array}-(CH_2)_m-$$

worin
$R^s$ und $R^{s'}$ unabhängig voneinander eine Alkyl- oder fluorsubstituierte Alkylgruppe mit 1 bis 10 Kohlenstoffatomen bedeuten, die Etherverbindungen zwischen Kohlenstoffatomen enthalten kann,
m mindestens 1 ist, und
p ein Anteilgewicht von 400 bis 10.000 vorsieht,
E und E' unabhängig voneinander ein polymerisierbares, ungesättigtes, organisches Radikal bedeuten, dargestellt durch die Formel:

$$R^{13}-CH=\overset{\displaystyle R^{12}\atop |}{C}-(CH_2)_w-(X)_x-(Z)_z-(Ar)_y-R^{14}-$$

worin
$R^{14}$ ein zweiwertiges Alkylenradikal mit 1 bis 10 Kohlenstoffatomen bedeutet,
$R^{12}$ H oder $CH_3$ bedeutet,
$R^{13}$ H, ein $(C_1-C_6)$ Alkylradikal oder eine $-CO-Y-R^{15}$-Gruppe, in der Y -O-, -S- oder -NH- ist und $R^{15}$ ein Alkylradikal mit 1 bis 12 Kohlenstoffatomen ist,
X -CO- oder -OCO- ist,
Z -O- oder -NH- ist,
Ar ein aromatisches Radikal mit 6 bis 30 Kohlenstoffatomen bedeutet,
w 0 bis 6 ist,
x 0 oder 1 ist,
y 0 oder 1 ist, und
z 0 oder 1 ist.

6. Eine Methode nach Anspruch 5, in der besagtes urethanhaltiges Prepolymer durch die folgende Formel dargestellt ist:



(IX)

worin

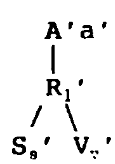
$R^{16}$ ein Diradikal eines Diisocyanats nach Beseitigung der Isocyanatgruppe ist und m, p und a genau wie vorher definiert sind.

7. Eine Methode nach irgendeinem vorhergehenden Anspruch, in der besagte Monomermischung N,N-Dimethylacrylamid und N-Vinylpyrrolidon enthält.

8. Eine Methode nach Anspruch 7, in der besagte Monomermischung entweder ein urethanhaltiges Prepolymer oder ein ethylenisch abgeschlossenes, polysiloxanhaltiqes Monomer enthält.

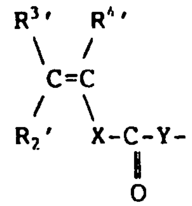
9. Eine Methode nach irgendeinem vorhergehenden Anspruch, in der besagte Monomermischung außerdem eine relativ nichtpolare, ringhaltige Zusammensetzung enthält, ausgewählt aus 2-Vinyl-4,4-dimethyl-2-oxazolin-5-on, 2-Isopropenyl-4,4-dimethyl-2-oxazolin-5-on, Cyclohexan-spiro-4'-(2'-isopropenyl-2'-oxazol-5'-on), Cyclohexan-spiro-4'-(2'-vinyl-2'-oxazol-5'-on) und 2-(1-Propenyl)-4,4-dimethyl-oxazon-5-on.

10. Eine Methode nach irgendeinem vorhergehenden Anspruch, in der besagte Monomermischung außerdem ein Vernetzungsmittel mit der folgenden allgemeinen schematischen Darstellung enthält:

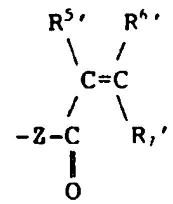


worin

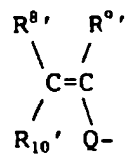
V folgendes bedeutet:



A' folgendes bedeutet:



S folgendes bedeutet:



$R_{1'}$ ein Alkylradikal ist, abgeleitet von substituierten und nichtsubstituierten Kohlenwasserstoffen, Polyalkylenoxid, Poly(perfluor) alkylenoxid, mit Dialkyl verkapptem Polydimethylsiloxan, mit Dialkyl verkapptem Polydimethylsiloxan, das mit Fluoralkyl- oder Fluorether-Gruppen modifiziert ist,
$R_{2'}$-$R_{10'}$ unabhängig voneinander H oder Alkyl mit 1 bis 5 Kohlenstoffatomen sind,
Q eine organische Gruppe ist, die aromatische Anteile mit 6 bis 30 Kohlenstoffatomen enthält,
X, Y und Z unabhängig voneinander 0, NH oder S sind,
v' 1 oder größer ist, und
a', s' unabhängig voneinander größer als oder gleich 0 sind und a' + s' ≥ 1.

11. Die Methode nach Anspruch 10, in der besagtes Vernetzungsmittel Methacryloxyethylvinylcarbonat ist.

12. Eine durch eine Methode nach irgendeinem vorhergehenden Anspruch gebildete silikonhaltige Hydrogelzusammensetzung.

13. Eine aus einer Hydrogelzusammensetzung nach Anspruch 12 hergestellte biomedizinische Vorrichtung.

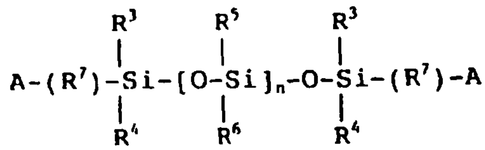
14. Eine Kontaktlinse nach Anspruch 13.

**Revendications**

1. Une méthode pour améliorer la mouillabilité des hydrogels contenant du silicone comprenant les étapes de (a) formation d'un mélange de monomères comprenant au moins un monomère contenant du silicone, N,N-diméthylacrylamide et un monomère contenant du vinyle sélectionné parmi N-vinylpyrrolidone, N-vinyle-N-méthyle acétamide, N-vinyle-N-éthyle acétamide, N-vinyle-N-méthyle formamide et N-vinyle formamide et (b) endurcissement du mélange de monomères de l'étape (a) pour former un hydrogel contenant du silicone présentant des propriétés de mouillabilité améliorées.

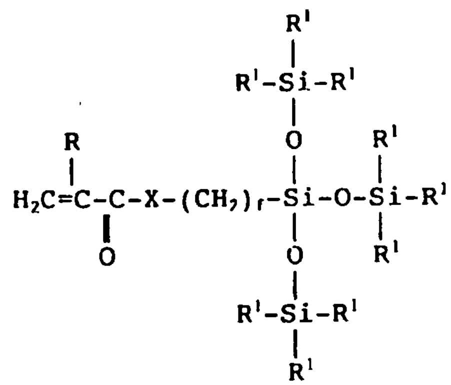
2. Une méthode conformément à la revendication 1, dans laquelle ledit monomère contenant du vinyle est N-vinylpyrrolidone.

3. Une méthode conformément à la revendication 1 ou à la revendication 2, dans laquelle ledit monomère contenant du silicone est un prépolymère contenant de l'uréthane; un prépolymère contenant un polysiloxane à terminaison éthylènique; un prépolymère poly (organosiloxane) représenté par la formule:



où

A est un groupe insaturé activé;
chaque $R^3$-$R^6$ est sélectionnée indépendamment à partir d'un radical hydrocarbure monovalent ou d'un radical hydrocarbure monovalent halogénosubstitué ayant 1 à 18 atomes de carbone pouvant avoir des liaisons éther entre les atomes de carbone;
$R^7$ est un radical hydrocarbure bivalent ayant de 1 à 22 atomes de carbone; et
n est 0 ou un nombre entier supérieur ou égal à 1; ou un monomère (méth)acrylique polysiloxanylalkyle volumineux de la formule:



où
X est O ou NR;
chaque R est indépendamment hydrogène ou méthyle; et
chaque $R^1$ est indépendamment un groupe alkyle ou phényle plus bas; et
f est 1 ou 3 à 10.

4. Une méthode conformément à la revendication 3, dans laquelle ledit monomère (méth)acrylique polysiloxanyalkyle volumineux est sélectionné parmi méthacryloxypropyle tris(triméthylsiloxy)silane, pentaméthyldisiloxanylméthylméthacrylate, tris(triméthylsiloxy)méthacryloxy propylsilane, phényltétraméthyldisiloxanyléthyle acétate, et methyldi(triméthylsiloxy)méthacryloxyméthyle silane.

5. Une méthode conformément à la revendication 3, dans laquelle ledit monomère contenant du silicone est un prépolymère contenant de l'uréthane de la représentation schématique suivante:

$$E(*D*A''*D*G)_a*D*A''*D*E';$$

ou

$$E(*D*G*D*A'')_a*D*G*D*E';$$

où

D indique un diradical alkyle, un diradical cycloalkyle alkyle, un diradical cycloalkyle, un diradical aryle ou un diradical alkylaryle ayant de 6 à 30 atomes de carbone;
G indique un diradical alkyle, un diradical cycloalkyle, un diradical cycloalkyle alkyle, un diradical aryle ou un diradical alkylaryle ayant de 1 à 40 atomes de carbone et qui peut contenir des liaisons éther, thio ou amine dans la chaîne principale;
* indique une liaison uréthane ou uréido;
a est au moins 1;
A" indique un radical polymère divalent de la formule:

$$-(CH_2)_m-\left[\begin{array}{c}R^s\\ |\\ -Si-O-\\ |\\ R^{s'}\end{array}\right]_p-\begin{array}{c}R^s\\ |\\ Si\\ |\\ R^{s'}\end{array}-(CH_2)_m-$$

où

$R^s$ et $R^{s'}$ indiquent indépendamment un groupe alkyle ou alkyle fluorosubstitué pouvant avoir des liaisons ether entre les atomes de carbone ayant de 1 à 10 atomes de carbone;

m est au moins 1 et

p fournit une portion en poids de 400 à 10.000;

E et E' indiquent indépendamment un radical organique insaturé polymérisable représenté par la formule:

$$R^{13}-CH=\overset{\overset{\displaystyle R^{12}}{|}}{C}-(CH_2)_w-(X)_x-(Z)_z-(Ar)_y-R^{14}-$$

où:

$R^{14}$ indique un radical alkylène divalent ayant de 1 à 10 atomes de carbone;

$R^{12}$ indique H ou $CH_3$;

$R^{13}$ indique H, un radical alkyle ($C_1$-$C_6$) ou un groupe -CO-Y-$R^{15}$ où Y est -O-, -S- ou -NH- et $R^{15}$ est un radical alkyle ayant de 1 à 12 atomes de carbone;

X est -CO- ou -OCO-;

Z est -O- ou -NH-;

Ar indique un radical aromatique ayant de 6 à 30 atomes de carbone;

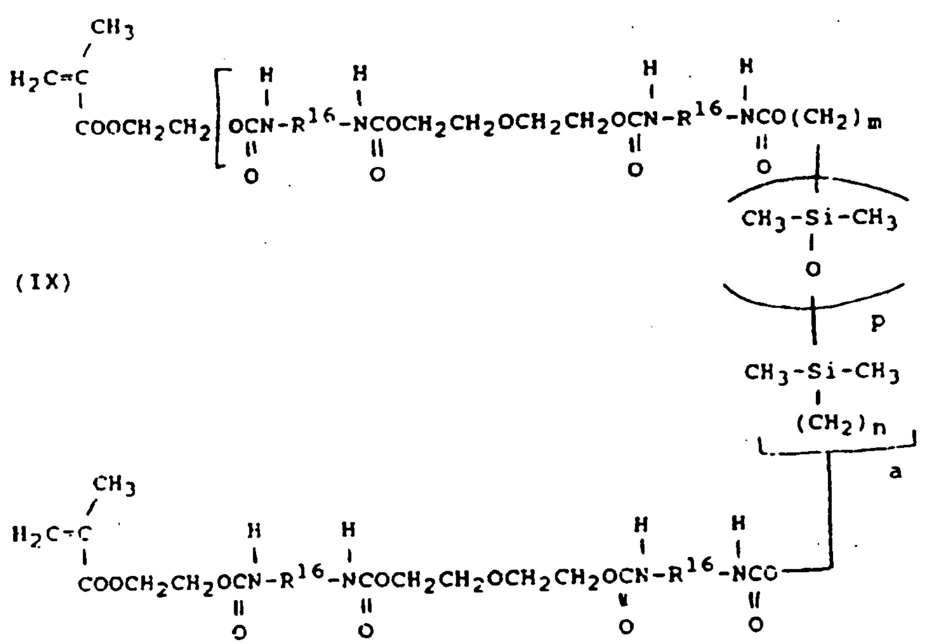
w est 0 à 6;

x est 0 ou 1;

y est 0 ou 1; et

z est 0 ou 1.

6. Une méthode conformément à la revendication 5, dans laquelle ledit prépolymère contenant de l'uréthane est représenté par la formule:



(IX)

où

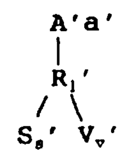
$R^{16}$ est un diradical d'lin diisocyanate après élimination du groupe isocyanate et m, p et a sont comme défini précédemment.

7. Une méthode conformément à l'une des revendications précédentes, dans laquelle ledit mélange de monomères comprend N,N-diméthylacrylamide et N-vinyle pyrrolidone.

8. Une méthode conformément à la revendication 7 dans laquelle ledit mélange de monomères comprend soit un prépolymère contenant de l'uréthane soit un monomère contenant polysiloxane à terminaison éthylènique.

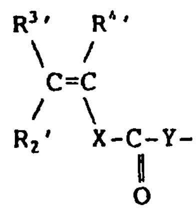
9. Une méthode conformément à l'une des revendications précédentes, dans laquelle ledit mélange de monomères comprend aussi un composé contenant une boucle relativement non polaire sélectionné parmi 2-vinyle-4,4-diméthyle-2-oxazoline-5-one, 2-isopropenyle-4,4-diméthyle-2-oxazoline-5-one,cyclohexane-spiro-4'-(2'-isopropenyl-2'-oxaxol-5'-one) , cyclohexane-spiro-4'-(2'-vinyle-2'-oxazol-5'-one) et 2-(1-propenyl)-4,4-diméthyle-oxazol-5-one.

10. Une méthode conformément à l'une des revendications précédentes, dans laquelle ledit mélange de monomères comprend également un agent de réticulation de la représentation schématique générale suivante:

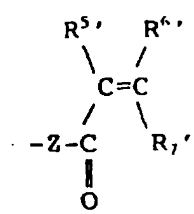


dans laquelle:

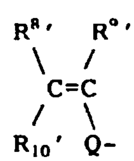
V indique



A' indique



S indique



$R_{1'}$ est un radical alkyle dérivé des hydrocarbures substitués et non substitués, oxyde polyalkylène, oxyde poly(perfluoro)alkylène, polydiméthylsiloxane à terminaison dialkyle, polydiméthylsiloxane à terminaison dialkyle modifié par des groupes fluoroalkyle ou fluoroéther;
$R_{2'}$-$R_{10'}$ sont indépendamment H ou alkyle avec 1 à 5 atomes de carbone;
Q est un groupe organique contenant des portions aromatiques ayant de 6 à 30 atomes de carbone;
X, Y et Z sont indépendamment O, NH ou S;

v' est 1 ou supérieur; et
a', s' indépendamment sont supérieurs ou égaux à 0 et a' + s' $\geq$ 1.

11. La méthode de la revendication 10, dans laquelle ledit agent de réticulation est carbonate vinyle méthacryloxyéthyle.

12. Une composition d'hydrogel contenant du silicone formée par une méthode conformément à l'une des précédentes revendications.

13. Un dispositif biomédical fait à partir d'une composition d'hydrogel telle que revendiquée à la revendication 12.

14. Une lentille de contact conformément à la revendication 13.

FIG. 1

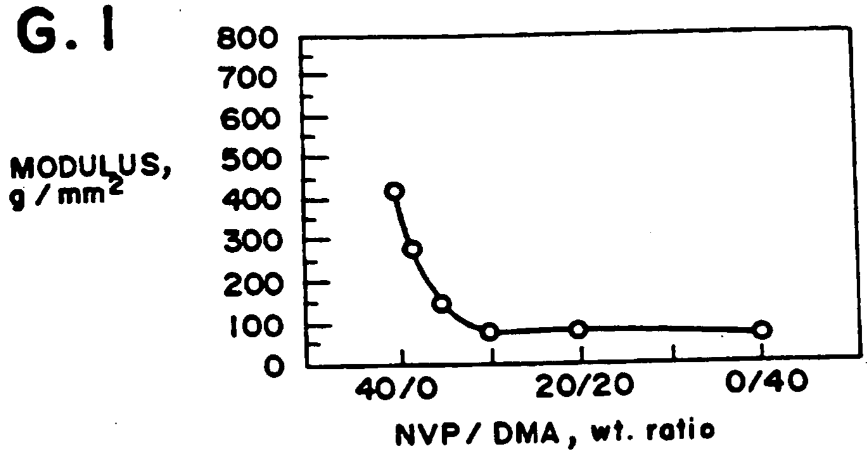



FIG. 2

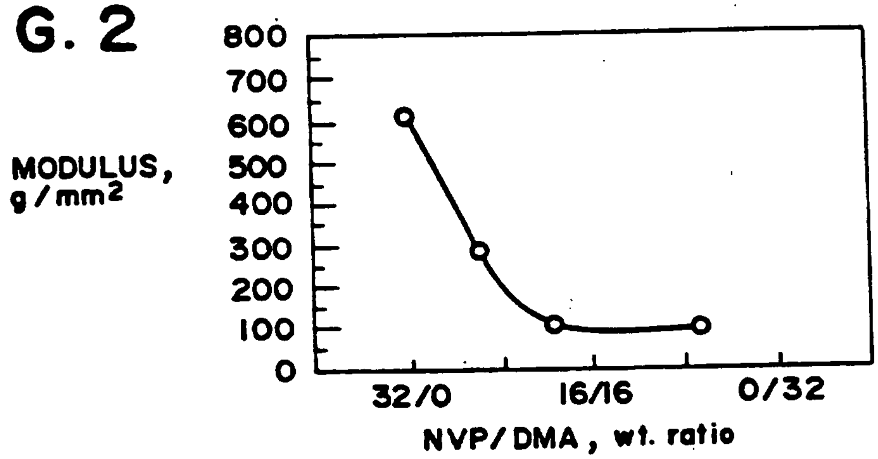



FIG. 3